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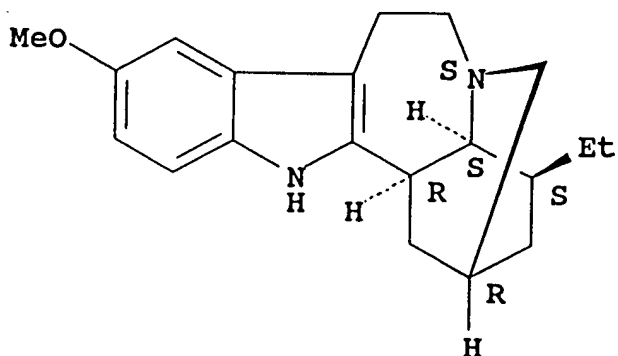
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=> d ide can 15

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1994 ACS
RN 83-74-9 REGISTRY
CN Ibogamine, 12-methoxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine
deriv. (9CI)
CN Ibogaine (7CI, 8CI)
OTHER NAMES:
CN (-)-Ibogaine
CN Ibogain
FS STEREOSEARCH
DR 17378-46-0
MF C20 H26 N2 O
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD,
CEN, CHEMLIST, CIN, CSCHM, DDR, DRUGNL, DRUGR, DRUGU,
DRUGUPDATES, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,
MRCK*, NAPRALERT, PNI, PROMT, SPECINFO, TOXLINE, TOXLIT
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
DES 4:.IBOGAMINE

Absolute stereochemistry.



L22
L23
L24

75 S L5 OR L18
81529 S METABOLITE#
8 S L22 AND L23

FILE 'WPIDS' ENTERED AT 12:11:40 ON 14 OCT 94

L25
L26
L27

8 S L18
1748 S METABOLITE#
0 S L25 AND L26

FILE 'HCA, HCAPREVIEWS, BIOSIS, EMBASE' ENTERED AT 12:12:37 ON 14 OCT 94

L28

12 DUP REMOVE L14 L16 L24 L21 (15 DUPLICATES REMOVED)

=> fil hca hcaprev biosis embase

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=> d 1-12 128 bib ab

✓L28 ANSWER 1 OF 12 BIOSIS COPYRIGHT 1994 BIOSIS

AN 94:410600 BIOSIS

DN 97423600

TI Evidence that ibogaine releases dopamine from the cytoplasmic pool in isolated mouse striatum.

AU Harsing L G Jr; Ser Shen H; Lajtha A

CS Cent. Neurochem., Nathan Kline Inst. Psychiatric Res., Orangeburg, NY 10962, USA

SO Journal of Neural Transmission General Section 96 (3). 1994. 215-225.

LA English

AB

We measured the effect of ibogaine on the tritium efflux from isolated mouse striatum preloaded with (3H)dopamine ((3H)DA). Ibogaine increased the basal tritium outflow in a concentration-dependent manner, but it was without effect on electrical stimulation-induced tritium overflow. Separation of the released radioactivity after ibogaine administration showed that this drug increased the release of (3H)DA and (3H)-dihydroxyphenylacetic acid ((3H)DOPAC), but the efflux of O-methylated-deaminated metabolites was not changed. The dopamine (DA)-releasing effect of ibogaine was reduced by the DA uptake inhibitors cocaine and nomifensine. The tritium efflux

evoked by ibogaine was not altered by omission of Ca^{2+} from the perfusion buffer or by inhibition of the voltage-sensitive Na^+ channels with tetrodotoxin. Ibogaine maintained its effect on release from superfused striatum prepared from reserpine-pretreated mice. The ibogaine-induced tritium release measured from mouse striatum that was preloaded with $(3\text{H})\text{DA}$ was not affected by the D-2 DA receptor ligands $(-)$ -quinpirole and $(+/-)$ -sulpiride, indicating that the ibogaine-induced release is not subject to presynaptic autoreceptor regulation. Ibogaine failed to affect $(3\text{H})\text{DA}$ uptake and retention in mouse striatum. These data indicate that at the nerve terminal level ibogaine releases DA, and the primary source for the release is probably the cytoplasmic pool. The DA-releasing effect of ibogaine may have importance in mediation of its hallucinogenic action, as seen in a frequent practice in African cults.

ANSWER 2 OF 12 EMBASE COPYRIGHT 1994 ELSEVIER SCI. B.V.

94206613 EMBASE

Evidence that ibogaine releases dopamine from the cytoplasmic pool in isolated mouse striatum.

Harsing L.G. Jr.; Sershen H.; Lajtha A.

Center for Neurochemistry, Nathan Kline Inst Psychiatric Res, Orangeburg, NY 10962, United States

J. NEURAL TRANSM. GEN. SECT., (1994) 96/3 (215-225).

ISSN: 0300-9564 CODEN: JNTMAH

Austria

Journal

008 Neurology and Neurosurgery

030 Pharmacology

037 Drug Literature Index

LA English

SL English

AB

We measured the effect of ibogaine on the tritium efflux from isolated mouse striatum preloaded with $[3\text{H}]\text{dopamine}$ ($[3\text{H}]\text{DA}$).

Ibogaine increased the basal tritium outflow in a concentration-dependent manner, but it was without effect on electrical stimulation-induced tritium overflow. Separation of the released radioactivity after ibogaine administration showed that this drug increased the release of $[3\text{H}]\text{DA}$ and $[3\text{H}]\text{-dihydroxyphenylacetic acid}$ ($[3\text{H}]\text{DOPAC}$), but the efflux of O-methylated-deaminated metabolites was not changed. The dopamine (DA)-releasing effect of ibogaine was reduced by the DA uptake inhibitors cocaine and nomifensine. The tritium efflux evoked by ibogaine was not altered by omission of Ca^{2+} from the perfusion buffer or by inhibition of the voltage-sensitive Na^+ channels with tetrodotoxin. Ibogaine maintained its effect on release from superfused striatum prepared from reserpine-pretreated mice. The ibogaine-induced tritium release measured from mouse-striatum that was preloaded with $[3\text{H}]\text{DA}$ was not affected by the D-2 DA receptor ligands $(-)$ -quinpirole and $(+/-)$ -sulpiride, indicating that the ibogaine-induced release is not subject to presynaptic autoreceptor regulation. Ibogaine failed to affect $[3\text{H}]\text{DA}$ uptake and retention in mouse striatum. These data indicate that at the nerve terminal level

ibogaine releases DA, and the primary source for the release is probably the cytoplasmic pool. The DA-releasing effect of ibogaine may have importance in mediation of its hallucinogenic action, as seen in a frequent practice in African cults.

- ✓ L28 ANSWER 3 OF 12 CAPREVIEWS COPYRIGHT 1994 ACS DUPLICATE 1
- AN 94:485878 CAPREVIEWS
- TI Effects of iboga alkaloids on morphine and cocaine self-administration in rats: relationship to tremorigenic effects and to effects on dopamine release in nucleus accumbens and striatum
- AU Glick, S. D.; Kuehne, M. E.; Raucci, J.; Wilson, T. E.; Larson, D.; Keller, R. W. Jr.; Carlson, J. N.
- CS Department of Pharmacology and Toxicology (A-136), Albany Medical College and the Capital District Center for Drug Abuse Research and Treatment, Albany, NY, 12208, USA
- SO Brain Res. (1994), 657(1-2), 14-22
- CODEN: BRREAP; ISSN: 0006-8993
- DT Journal
- LA English
- AB Ibogaine, a naturally occurring alkaloid, has been claimed to be effective in treating addiction to opioid and stimulant drugs and has been reported to decrease morphine and cocaine self-administration in rats. The present study sought to determine if other iboga alkaloids, as well as the chemically related harmala alkaloid harmaline, would also reduce the i.v. self-administration of morphine and cocaine in rats. Because both ibogaine and harmaline induce tremors, an effect that may be causally related to neurotoxicity in the cerebellar vermis, the tremorigenic activities of the other iboga alkaloids were assessed. Lastly, in view of the involvement of the dopaminergic mesolimbic system in the actions of drugs of abuse, the effects of some of the iboga alkaloids on extracellular levels of dopamine and its metabolites in the nucleus accumbens and striatum were determined. All of the tested alkaloids (i.e., ibogaine, tabernanthine, R- and S-coronaridine, R- and S-ibogamine, desethylcoronaridine, and harmaline) dose-dependently (2.5-80 mg/kg) decreased morphine and cocaine intake in the hour after treatment; decreases in morphine and cocaine intake were also apparent the day after administration of some but not all of these alkaloids (i.e., ibogaine, tabernanthine, desethylcoronaridine, and the R-isomers of coronaridine and ibogamine). In some rats, there were persistent decreases in morphine or cocaine intake for several days after a single injection or after two or three weekly injections of one or another of these alkaloids; R-ibogamine produced such effects more consistently than any of the other alkaloids. At the doses used to assess effects on drug self-administration, ibogaine, tabernanthine, desethylcoronaridine and harmaline all induced tremors for at least 2-3 h; both enantiomers of both coronaridine and ibogamine induced very weak or no tremors. Using *in vivo* microdialysis, the effects of the R- and S-enantiomers of coronaridine and ibogamine on extracellular dopamine levels in the nucleus accumbens and striatum were compared. The R-enantiomers decreased dopamine levels in both brain regions whereas the

S-enantiomers produced no significant changes in dopamine levels in either region. The results of this study indicate that the 'anti-addictive' and tremorigenic effects of the iboga alkaloids can be dissociated and that long-term effects of these alkaloids in drug self-administration appear to be related to initial decreases in dopaminergic activity in specific brain areas.

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ANSWER 4 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 2
119:262348 CA

TI Inhibitory effects of ibogaine on cocaine self-administration in rats

AU Cappendijk, Susanne L. T.; Dzoljic, Michailo R.

CS Fac. Med. Health Sci., Erasmus Univ. Rotterdam, Rotterdam, 3000 DR, Neth.

SO Eur. J. Pharmacol. (1993), 241(2-3), 261-5

DT CODEN: EJPHAZ; ISSN: 0014-2999

LA Journal

AB English

In order to determine the potential antiaddictive properties of ibogaine, the cocaine self-administration model was used in rats. A single injection of ibogaine (40 mg/kg i.p.) produced a decrease of cocaine intake, which lasted for >48 h. Since the half-life time of ibogaine is short, this might suggest the involvement of one or several active metabolites of ibogaine in regulating cocaine intake. Repetitive administration of ibogaine on 3 consecutive days also induced a pronounced decrease of cocaine intake. However, a more prominent inhibitory effect on cocaine intake was observed in animals treated repeatedly with ibogaine, 40 mg/kg i.p. once each week for 3 consecutive weeks. These results indicate that ibogaine or its metabolite(s) is a long-lasting interruptor of cocaine dependence, which supports similar observations from uncontrolled clinical studies.

L28
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TI

ANSWER 5 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 3
120:69440 CA

TI Local effects of ibogaine on extracellular levels of dopamine and its metabolites in nucleus accumbens and striatum: interactions with D-amphetamine

AU Glick, S. D.; Rossman, K.; Wang, S.; Dong, N.; Keller, R. W. Jr.

CS Department of Pharmacology and Toxicology (A-136), and the Capital

District Center for Drug Abuse Research and Treatment, Albany

SO Medical College, New Scotland Avenue, Albany, NY, 12208, USA

DT Brain Res. (1993), 628(1-2), 201-8

LA CODEN: BRREAP; ISSN: 0006-8993

AB Journal

English

AB Systemic administration of ibogaine (40 mg/kg, i.p.) has

been reported to induce both acute (1-3 h) and persistent (19-20 h) changes in extracellular levels of dopamine and its

metabolites in the nucleus accumbens and striatum. In the

present study, local administration of ibogaine to the

striatum and nucleus accumbens produced effects that mimicked both

the acute and persistent effects of systemic administration:

perfusion with high concns. (200 and 400 .mu.M) of ibogaine mimicked the acute effects (decreased extracellular dopamine levels and increased extracellular metabolite levels) whereas perfusion with a low concn. (10 .mu.M) of ibogaine mimicked the persistent effects (decreased extracellular levels of DOPAC). These results indicate that ibogaine acts directly in brain regions contg. dopaminergic nerve terminals and that long-lasting effects of systemically administered ibogaine might be mediated by persisting low levels of ibogaine. Locally administered ibogaine (10 .mu.M) was also found to enhance the effects of systemically administered D-amphetamine (1.25 mg/kg, i.p.) on extracellular dopamine levels, and conversely, systemically administered ibogaine (40 mg/kg, i.p.; 19 h pretreatment) enhanced the effects of locally administered D-amphetamine (1-10 .mu.M). These results indicate that, in addn. to a metabolic mechanism implicated previously, a pharmacodynamic mechanism contributes to the interaction between ibogaine and D-amphetamine. The relevance of such mechanisms to claims regarding ibogaine's anti-addictive properties is unclear.

ANSWER 6 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 4
 116:166169 CA
 TI Ibogaine antagonizes cocaine-induced locomotor stimulation in mice
 AU Sershen, Henry; Hashim, Audrey; Harsing, Laszlo; Lajtha, Abel
 CS Div. Neurochem., Nathan S. Kline Inst., Orangeburg, NY, 10962, USA
 SO Life Sci. (1992), 50(15), 1079-86
 CODEN: LIFSAB; ISSN: 0024-3205
 DT Journal
 LA English
 AB

Ibogaine (40 mg/kg i.p.), when given 2 h before an acute injection of cocaine (25 mg/kg s.c.) to C57BL/6 mice, reduced the cocaine-induced locomotor stimulation. Such stimulation was also reduced in the ibogaine-treated mice when a second injection of cocaine was given 24 h later. Thus, the redn. in locomotor activity was not just the short-term depression of locomotor activity seen after ibogaine administration. When mice were given a daily injection of cocaine for 3 days and ibogaine was given after the cocaine injection on day 3, and again on day 4, cocaine-induced locomotor activity was reduced three hours later on day 4. On days 5 and 9 of the cocaine administration, with no further ibogaine treatment ambulatory counts were still lower in the ibogaine-pretreated mice. Locomotor stimulation induced by amphetamine (10 mg/kg) was not affected by ibogaine. An acute injection of ibogaine resulted in a transient increase in turnover of dopamine, as indicated by the increase in the ratio of metabolites of the dopamine to dopamine, followed by a decrease in the metabolites in striatum and frontal cortex 24 h later. In vivo treatment with ibogaine did not affect the binding of [³H]WIN 35,248 to the cocaine binding site in striatal tissue measured in vitro. In addn., ibogaine added in vitro had a weak affinity to the WIN 35,248 binding site (IC50 for cocaine = 120 nM and for ibogaine = 1,500 nM).

The results suggest that ibogaine may have induced a selective change in the dopaminergic system that results in a decrease in responsiveness to cocaine that persisted for at least 1 wk.

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ANSWER 7 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 5
117:163813 CA
Ibogaine reduces amphetamine-induced locomotor stimulation in C57BL/6By mice, but stimulates locomotor activity in rats Sershen, Henry; Harsing, Laszlo G., Jr.; Hashim, Audrey; Lajtha, Abel
Div. Neurochem., Nathan S. Kline Inst. Psychiatr. Res., Orangeburg, NY, 10962, USA
Life Sci. (1992), 51(13), 1003-11
CODEN: LIFSAR; ISSN: 0024-3205
Journal
English

The effect of ibogaine hydrochloride on locomotor stimulation induced by d-amphetamine sulfate was tested in male C57BL/6By mice and in female Sprague-Dawley rats. In mice, locomotor stimulation induced by d-amphetamine at 1 or 5 mg/kg s.c. was reduced by prior administration of one or two injections of ibogaine (40 mg/kg), given 2 or 18 h earlier. This reductn. in locomotor activity persisted for two days. Locomotor stimulation induced by a higher dose (10 mg/kg) of d-amphetamine was not reduced by such prior administration of ibogaine. A lower dose of ibogaine (20 mg/kg) did not reduce the subsequent locomotor activity induced by d-amphetamine. Ibogaine decreased striatal dopamine levels, while d-amphetamine increased them. Ibogaine treatment (2 times. 40 mg/kg, 18 h apart) induced a decrease by 30% in the level of striatal dopamine and its metabolites measured in tissue exts. 3 h after the second ibogaine injection. One hour after d-amphetamine (5 mg/kg) administration, the level of striatal dopamine increased by 26%. Although the level of striatal dopamine was initially lower in the ibogaine-pretreated mice, d-amphetamine (5 mg/kg) administration induced an increase in striatal dopamine and its metabolites. The effect of ibogaine seems to be species specific, since in rats pretreated with ibogaine 18 h before d-amphetamine, locomotor stimulation induced by d-amphetamine was further increased. In addn., the in vitro elec.-evoked release of [³H]dopamine from striatal tissue was either unchanged or inhibited in the presence of d-amphetamine, and after ibogaine pretreatment in vivo, the release of tritium in the presence of d-amphetamine was inhibited or stimulated in mice and rats, resp.

✓L28
AN
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ANSWER 8 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 6
116:143736 CA
Mechanisms of action of ibogaine and harmaline congeners based on radioligand binding studies
Decher, Darlene C.; Teitler, Milton; Soderlund, David M.; Bornmann, William G.; Kuehne, Martin; Glick, Stanley D.
Dep. Pharmacol. Toxicol., Albany Med. Coll., Albany, NY, 12208, USA

SO Brain Res. (1992), 571(2), 242-7
CODEN: BRREAP; ISSN: 0006-8993

DT Journal

English

AB Assays U

Assays using radioligands were used to assess the actions of ibogaine and harmaline on various receptor types. Whereas harmaline and harmine showed affinity for opiate receptors 2.0 μ M at μ -opiate receptors. The K_i for coronaridine was tabernanthine at the δ -opiate receptors were 8.1 and 3.1 μ M, resp. Ibogaine, ibogamine, coronaridine, and tabernanthine had K_i values of 2.08, 2.6, 4.3 and 0.15 μ M, resp., for κ -opiate receptors. Long-lasting, dose-dependent behavioral effects of ibogaine have been reported. The possibility that these effects were due to irreversible binding properties of ibogaine at κ -receptors was considered; however, radioligand wash expts. showed a rapid recovery of radioligand binding after one wash. A voltage-dependent sodium channel radioligand demonstrated K_i values in the μ M range for all drugs tested. Using radioligand binding assays and/or 36Cl-uptake studies, no interaction of ibogaine or harmaline with the GABA receptor-ionophore was found. The κ -activity of ibogaine (or an active metabolite) may be responsible for its putative anti-addictive properties whereas the tremorigenic properties of ibogaine and harmaline may be due to their effects on sodium channels.

✓L28

/L28 ANSWER 9 OF 12 CA COPYRIGHT 1994 ACS

AN 116:248274 CA

DUPLICATE 7

TTI Acute and prolonged effects of ibogaine on brain dopamine metabolism
and morphine-induced locomotor activity in rats
MAU Maisonneuve, I. M.; Rossman, K. L.; Keller, R. W., Jr.; Glick, S. D.
CCS Dep. Pharmacol. Toxicol., Albany Med. Coll., Albany, NY, 12208, USA
SO Brain Res. (1992), 575(1), 69-73
CODEN: BRREAP; ISSN: 0006-8993

OT Journal

English

AB Iboqaine

Ibogaine, an indoalkylamine, proposed for use in treating opiate and stimulant addiction, has been shown to modulate the dopaminergic system acutely and one day later. In the present study, the authors sought to systematically determine the effects of **Ibogaine** on the levels of dopamine (DA) and the dopamine metabolites 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) in tissue at several time points, between 1 h and 1 mo post-injection. One hour after **ibogaine** administration (40 mg/kg i.p.), a 50% decrease in DA along with a 37-100% increase in HVA were observed in all 3 brain regions studied: striatum, nucleus accumbens and prefrontal cortex. Nineteen hours after **ibogaine** administration, a decrease in DOPAC was seen in the nucleus accumbens and in the striatum. A week after administration of **ibogaine**, striatal DOPAC levels were still reduced. A month after **ibogaine** injection there were no significant neurochemical changes in any region. The authors also investigated the effects of **ibogaine** pretreatment on

morphine-induced locomotor activity, which is thought to depend on DA release. Using photocell activity cages, it was found that ibogaine pretreatment decreased the stimulatory motor effects induced by a wide range of morphine doses (0.5-20 mg/kg i.p.) administered 19 h later; a similar effect was obsd. when morphine (5 mg/kg) was administered a week after ibogaine pretreatment. No significant changes in morphine-induced locomotion were seen a month after ibogaine pretreatment. The present findings indicate that ibogaine produces both acute and delayed effects on the tissue content of DA and its metabolites, and these changes coincide with a sustained depression of morphine-induced locomotor activity.

✓L28 ANSWER 10 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 8

AN 115:64663 CA

TI Interactions between ibogaine, a potential anti-addictive agent, and morphine: an in vivo microdialysis study

AU Maisonneuve, I. M.; Keller, R. W., Jr.; Glick, S. D.

CS Dep. Pharmacol. Toxicol., Albany Med. Coll., Albany, NY, 12208, USA

SO Eur. J. Pharmacol. (1991), 199(1), 35-42

CODEN: EJPHAZ; ISSN: 0014-2999

DT Journal

LA English

AB

The indolalkylamine ibogaine may be effective in abolishing drug craving in heroin and cocaine addicts. In vivo microdialysis was used to det. the effects of ibogaine on brain extracellular levels of dopamine (DA) and its metabolites and the effects of ibogaine

pretreatment on morphine stimulation of brain DA systems.

Ibogaine (40 mg/kg i.p.) decreased extracellular DA levels in the striatum, increased them in the prefrontal cortex, and had no effects in the nucleus accumbens. At 19 h after ibogaine injection, DA levels were still decreased in the striatum and the metabolite levels were lower in all 3 regions. When

injected 19 h prior to a morphine challenge (5 mg/kg i.p.), ibogaine (40 mg/kg, i.p.) prevented the rise in DA levels in

all 3 regions normally obsd. after a morphine injection. A high dose of morphine (30 mg/kg i.p.) alone produced no increase in extracellular DA levels. It is unclear whether ibogaine antagonized or potentiated the effects of the lower dose of morphine. Regardless of the nature of this interaction, ibogaine effects brain DA systems for a period of time that exceeds its elimination from the body. During this time ibogaine alters the responses of DA systems to morphine.

✓L28 ANSWER 11 OF 12 CA COPYRIGHT 1994 ACS

AN 110:87907 CA

TI Xenobiotic and endobiotic inhibitors of cytochrome P-450db1

AU Fonne-Pfister, Raymonde; Meyer, Urs A.

CS Biocent., Univ. Basel, Basel, CH-4056, Switz.

SO Biochem. Pharmacol. (1988), 37(20), 3829-35

CODEN: BCPN6; ISSN: 0006-2952

DT Journal

LA
AB

English

Five to 10% of Caucasians are poor metabolizers of debrisoquine, sparteine, bufuralol, and numerous other drugs. A deficiency in cytochrome P-450db1 (P-450db1) function is the cause of this polymorphism of drug oxidn., which has autosomal recessive inheritance. In the present study, inhibition of bufuralol-1'-hydroxylase in human liver microsomes by drugs and other chems. was tested in a search for potential new substrates for this polymorphic enzyme. Of the 80 alkaloids and drugs tested, 25 were competitive inhibitors. In vitro competitive inhibition of bufuralol oxidn. by a substance indicates that this compd. is able to bind to the same enzymic site as bufuralol. This may mean that the competing drug also is metabolized by P-450db1 and that its metab. is subject to the same genetic variation as the oxidn. of bufuralol. However, some of these competitive inhibitors are not oxidized by P-450db1. In this case, however, they may interfere with the in vivo phenotyping procedure by inhibiting the formation of metabolites of test drugs such as debrisoquine, sparteine, metoprolol, or dextromethorphan.

✓28

ANSWER 12 OF 12 CA COPYRIGHT 1994 ACS

AN 103:42702 CA

TI High-performance liquid chromatographic analysis of basic drugs on silica columns using non-aqueous ionic eluents. II. Application of UV, fluorescence and electrochemical oxidation detection

AU Jane, I.; McKinnon, A.; Flanagan, R. J.

CS Metrop. Police Forensic Sci. Lab., London, SE1 7LP, UK

SO J. Chromatogr. (1985), 323(2), 191-225

CODEN: JOCRAM; ISSN: 0021-9673

DT Journal

LA English

AB Unmodified silica columns together with nonaq. ionic luent give stable yet flexible systems for the anal. of basic drugs by HPLC. Low-wavelength UV and fluorescence detection may be used, and fluorescence may be optimized by, post-column pH change or derivatization of some primary aliph. amines with o-phthalaldehyde [643-79-8]. A novel feature is that electrochem. oxidn. can be used for the detection of most analytes and this detection mode is thus discussed in detail. Retention and relative response data (UV, 254 nm and electrochem., +1.2 V) were generated for 462 compds. using a 125-mm Spherisorb S5W silica column and methanolic NH₄ClO₄ (10 mM, pH 6.7) as eluent. This system can be used isocratically in qual. analyses and also for quant. work, when either the wavelength or the applied potential can be adjusted to optimize the response.

=> fil wpids

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FILE LAST UPDATED: 10 OCT 94

<941010/UP>

>>>UPDATE WEEKS:

MOST RECENT DERWENT WEEK

9433

DERWENT WEEK FOR CHEMICAL CODING: 9426

DERWENT WEEK FOR POLYMER INDEXING: 9430

<199433/DW>

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>>> DERWENT POLYMER INDEXING THESAURUS AVAILABLE IN FIELD /PLE <<<

>>> PATENT DRAWINGS AVAILABLE FOR PRINT AND DISPLAY <<<

0 => d 125 1-8 std ab

L25 ANSWER 1 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 92-007193 [01] WPIDS

DNC C92-003067

TI Treatment of poly-drug dependency - with ibogaine,
ibogamine or tabernanthine or their salts or deriv..

DC B02

IN LOTSOFF, H S

PA (NDAI-N) NDA INT INC; (LOTS-I) LOTSOFF H S

CYC 17

PI WO 9118609 A 911212 (9201)*
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: CA JP

US 5152994 A 921006 (9243) 4 pp A01N043-46

EP 511325 A1 921104 (9245) EN 15 pp A61K031-55

R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE

ADT US 5152994 A US 90-531100 900531; EP 511325 A1 EP 91-910992 910530,

WO 91-US3781 910530

FDT EP 511325 A1 Based on WO 9118609

PRAI US 90-511100 900531

IC ICM A01N043-46; A61K031-55

ICS A61K009-08; A61K009-48

AB WO 9118609 A UPAB: 931006

Treating poly-drug dependency comprises internal admin. of
ibogaine, ibogamine, tabernanthine, their therapeutically
active cpds., their salts, or a mixt., to a subject dependent on
heroin, cocaine, alcohol, caffeine, amphetamine, desoxyephedrine,
nicotine, methadone or other opiate narcotics in one or mor
combinations.

USE/ADVANTAGE - The method provides a high degree of success, with
craving either totally interrupted or reversal or modification
allowed, and is easy, convenient, rapid, acceptable to the addict
population. There is absence of pain, discomfort, undesirable or
persistent side effects. Effectiveness in the long term is good; a
single treatment, or a series, interrupted drug desire for 1-18
months or longer.

0/0

L25 ANSWER 2 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD

AN 91-207487 [28] WPIDS

DNC C91-089966

TI Treating nicotine-tobacco dependency - by administering alkaloid of
apocynaceae family on salt, e.g. ibogaine or ibogamine
hydrochloride.

DC B02 D18

IN LOTSOFF, H S

PA (NDAI-N) NDA INT INC

CYC 1

PI US 5026697 A 910625 (9128)*

ADT US 5026697 A US 90-530263 900530

PRAI US 90-530263 900530; US 90-580223 900910

IC A61K003-55

AB US 5026697 A UPAB: 930928

Method for treating nicotine/tobacco dependency comprises internal admin. of at least one Apolynaceae alkaloid (I) or its salt. USE/ADVANTAGE - The method gives rapid interruption of physical and psychological withdrawal symptoms associated with nicotine or tobacco abuse. Dosage is 1-60 mg/kg orally or rectally as a single repeated admin. with successive administrations spaced at a plurality. @ (4pp Dwg.No.0/0)

0 L25 ANSWER 3 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 89-300379 [41] WPIDS

DNN N89-229131 DNC C89-132881

TI Alcohol dependency and abuse treatment - comprises administering ibogaine and/or its non-toxic salts.

DC B02 P34

IN LOTSOFF, H S

PA (NDAI-N) NDA INT INC

CYC 1

PI US 4857523 A 890815 (8941)* 3 pp

ADT US 4857523 A US 88-221030 880718

PRAI US 88-221030 880718

IC A61U031-55

AB US 4857523 A UPAB: 930923

Treating alcohol dependency and abuse comprises internally administering a dosage of 4-25 mg/kg of ibogaine and/or its therapeutically active cpd.

The dosage is administered orally and the compsn. contains ibogaine and/or its hydro chloride or hydrobromide in a dosage of 400-1000 mg. The dosage is pref. in capsule, tablet, pill, powder or soln. form and is admixed with binders or fillers. A plurality of dosages are administered, intervals of a number of days intervening between successive dosages. A single treatment is effective for about 6 months.

USE/ADVANTAGE - The method is partic. for lessening the physiological and psychological aspects of alcohol habituation. It has a high degree of success, with the absence of pain and discomfort accompanying earlier treatments and is easy and convenient to use. There are no undesirable or persistent side effects and the invention is non-addicting and in a series of treatments will remove any potential for its own abuse.
0/0

/L25 ANSWER 4 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 86-137162 [21] WPIDS

DNC C86-058803

TI Interruption of cocaine and amphetamine abuse syndrome - using ibogaine or salts.

DC B02

PA (LOTS-I) LOTSOFF H S

CYC 1

PI US 4587243 A 860506 (8621)* 4 pp

ADT US 4587243 A US 85-754836 850715

PRAI US 85-754836 850715

IC A61K031-55

AB US 4587243 A UPAB: 930922

Method of treating cocaine and/or amphetamine abuse comprises admin. of ibogaine (I) and/or its therapeutically active cpd(s)., pref. a non-toxic salt, esp. HCl or HBr salt. Dose is pref. 6-19 mg/kg, pref. p.o., in units of 400-1000 mg.. Pref. admin. is spaced with a no. of days between successive doses.

ADVANTAGE - (I) disrupts the cocaine/amphetamine habituation syndrome, is not a euphoriant hallucinogen, and does not leave the subject open to swells of emotion. Treatment is effective and undesirable or persistent side-effects are absent.

0/0

✓L25 ANSWER 5 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD

AN 85-055920 [09] WPIDS

DNC C85-024345

TI Long lasting treatment of heroin addiction - by oral admin. of ibogaine (hydrochloride or hydrobromide salt).

DC B02

PA (LOTS-I) LOTSOFF H S

CYC 27

PI US 4499096 A 850212 (8509)* 4 pp

WO 8502115 A 850523 (8522) EN

RW: AT BE CF CG CH CM DE GA GB LU MR NL SE SN TD TG

W: AU DK FI JP

NO 8404573 A 850610 (8530)

AU 8436744 A 850603 (8535)

EP 163697 A 851211 (8550) EN

R: CH DE FR GB LI NL

DK 8503164 A 850711 (8713)

CA 1237986 A 880614 (8828)

EP 163697 B 900523 (9021)

R: CH DE FR GB LI NL

IL 73585 A 900429 (9026)

DE 3482305 G 900628 (9027)

IT 1178249 B 870909 (9035)

ADT US 4499096 A US 83-553138 831118; WO 8502115 A WO 84-US1851 841113

PRAI US 83-553138 831118

IC A61K031-43; A61K043-00; C07D471-18; C07D487-00

AB US 4499096 A UPAB: 930925

Heroin addiction may be treated by admin. of ibogaine (I) (or its deriv.) at a dosage of 6-19 mg/kg. Oral treatment using (I), its hydrochloride or hydrobromide, is also claimed.

ADVANTAGE - The method avoids the great pain and discomfort associated with prior art treatments, and does not show persistent side effects. A high degree of success in alleviating addiction is shown as there is rapid interruption of physiological and psychological withdrawal and the elimination of the addicts desire to use heroin for about six months. (I) itself is non-addicting, and

in a series of treatments will remove its own potential for abuse.
o/o

L25 ANSWER 6 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 73-10754U [08] WPIDS
TI 10-methoxyibogamine formyl and acetyl derivs - - as analgetic and anti-inflammatory agents.
DC B02
PA (AMCY) AMERICAN CYANAMID CO
CYC 1
PI US 3715361 A (7308)*
PRAI US 71-187895 711008
IC C07D043-38
AB US 3715361 A UPAB: 930831
New ibogamine derivs. of formula: (where (I) R = CHO, R1 = R" = H, (II) R1 = CHO, R = R" = H, (III) R1 = CHO, R = H, R" = CH3 and (IV) R1 = R" = COCH3, R = H) and their non-toxic acid addition salts are useful as analgetic and anti-inflammatory agents. I, II and III are prepared from 10-methoxyibogamine (ibogaine) by formylation using the Vilsmeier-Hack reaction or a modification of it and (IV) is prepared by acetylating ibogaine with acetic acid, acetic anhydride and BF3.

✓ L25 ANSWER 7 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 66-39590F [00] WPIDS
TI Amphetamine mixed with tabernanthe iboga alkaloids.

DC B00
PA (BOCH) BOCHER DPM
CYC 5
PI BE 726760 A (6800)*
DE 1902227 A (6801)
FR 7131 M (7046)
GB 1256914 A (7149)
CA 939266 A (7402)
PRAI FR 68-138081 680131
AB BE 726760 A UPAB: 930831

The association of amphetamine or one of its derivs. with an alkaloid extract of Tabernanthe iboga, a total extract of this plant, or pure ibogaine.

Useful in psychotherapy. The alkaloids clear the thought of the patient, giving him an extra-lucid vision of hims lf, and assisting him to remember his early life before the age of 4. The amphetamine brings a stimulation of the emotions to balance the intellectual stimulation. The use of this treatment may shorten the course of treatment considerably.

L25 ANSWER 8 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 66-00948F [00] WPIDS
TI Analgesic comps.

DC B00
PA (CIBA) CIBA LTD
CYC 1
PI GB 841697 A (6800)*
AB GB 841697 A UPAB: 930831

Analgesics of the morphine series such as morphine, codeine, codeine derivatives, dihydro-morphinone, methyl-dihydromorphinone, pantopon, ethylmorphine, -ketobemidone, meperidine, dihydrocodeinone, dihydromorphine, dihydro-desoxymorphine-D, dihydroscodeine-D, dl-3-methoxy-N-methyl-morphinan and dl-3-hydroxy-N-methylmorphinan are potentiated with ibogaine or tavern-xanthine. The latter are indole alkaloids isolated from the plant Tabernanthe Iboga. The weight ratio of alkaloid: narcotic is 0.5-20:1

=>
=>
=>

=> fil reg

FILE 'REGISTRY' ENTERED AT 12:17:48 ON 14 OCT 94
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STRUCTURE FILE UPDATES: 8 OCT 94 HIGHEST RN 158188-97-7
DICTIONARY FILE UPDATES: 13 OCT 94 HIGHEST RN 158188-97-7

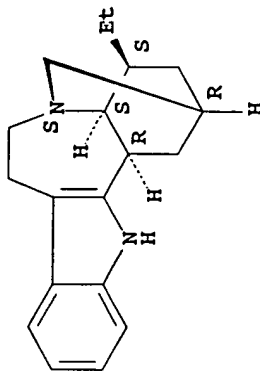
TSCA INFORMATION NOW CURRENT THROUGH MAY 1994

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

=> d ide can 14

✓L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1994 ACS
RN 481-87-8 REGISTRY
CN Ibogamine (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine
deriv. (9CI)
OTHER NAMES:
CN (-)-Ibogamine
CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole,
7-ethyl-6,6a,7,8,9,10,12,13-octahydro-, [6R-
(6.alpha.,6a.beta.,7.beta.,9.alpha.)]-
CN Ibogamin
CN [6R-(6.alpha.,6a.beta.,7.beta.,9.alpha.)]-7-Ethyl-
6,6a,7,8,9,10,12,13-octahydro-6,9-methano-5H-
pyrido[1',2':1,2]azepino[4,5-b]indole
FS STEREOSEARCH
MF C19 H24 N2
CI COM
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD,
CHEMINFORMRX, DDR, DRUGR, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB,
IPA, NAPRALERT, SPECINFO, TOXLINE, TOXLIT
(*fil contains numerically searchable property data)
DES 4:..IBOGAMINE

Absolute stereochemistry.



57 REFERENCES IN FILE CA (1967 TO DATE)
 4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 30 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 116:143736
 REFERENCE 2: P 116:100980
 REFERENCE 3: 116:55592
 REFERENCE 4: 116:37986
 REFERENCE 5: P 116:17031
 REFERENCE 6: 112:155225
 REFERENCE 7: 110:189357
 REFERENCE 8: 110:154646
 REFERENCE 9: 109:122005
 REFERENCE 10: 108:204858

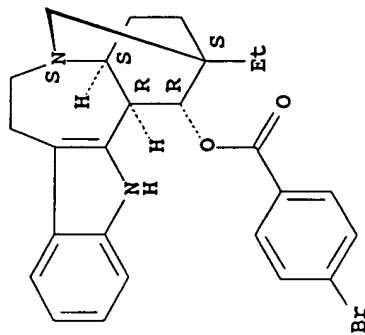
=>

=> d ide can 13 1-8

✓13 ANSWER 1 OF 8 REGISTRY COPYRIGHT 1994 ACS
 RN 88660-09-7 REGISTRY
 CN 20,21-Dinoribogamin-1-ol, 2-ethyl-, 4-bromobenzoate (ester),
 (1.alpha.)-(.+-.)- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN 6,9-Methano-5H-pyrindo[1',2':1,2]azepino[4,5-b]indole,
 20,21-dinoribogamin-1-ol deriv. (9CI)
 OTHER NAMES:
 CN (.+-.)-16-Hydroxy-allo-ibogamine p-bromobenz ate
 PS STEREOSEARCH

MF C26 H27 Br N2 O2
 LC STN Files: CA
 DES 3:(+)-4:1A.IBOGAMINE

Racemate. One enantiomer shown.



1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 100:64969

✓L3 ANSWER 2 OF 8 REGISTRY COPYRIGHT 1994 ACS
 RN 88660-07-5 REGISTRY
 CN 20,21-Dinoribogamin-1-ol, 2-ethyl-, (1.alpha.)-(.-.-.)- (9CI) (CA INDEX NAME)

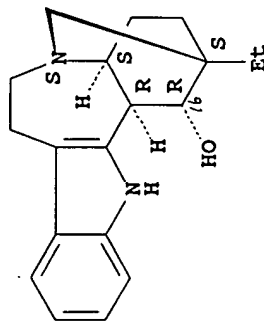
OTHER CA INDEX NAMES:

CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole,
 20,21-dinoribogamin-1-ol deriv. (9CI)

OTHER NAMES:

CN (.-.-.)-16-Hydroxy-allo-ibogamine
 FS STEREOSEARCH
 MF C19 H24 N2 O
 LC STN Files: CA
 DES 3:(+)-4:1A.IBOGAMINE

Racemate. One enantiomer shown.



1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 100:64969

JL3 ANSWER 3 OF 8 REGISTRY COPYRIGHT 1994 ACS
 RN 77123-15-0 REGISTRY
 CN Ibogamine-18-carboxylic acid, 19-hydroxy-, methyl ester, (19S)-

(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole,
 ibogamine-18-carboxylic acid deriv. (9CI)

OTHER NAMES:

CN (19S)-Hydroxycoronaridine

CN (3S)-Hydroxycoronaridine

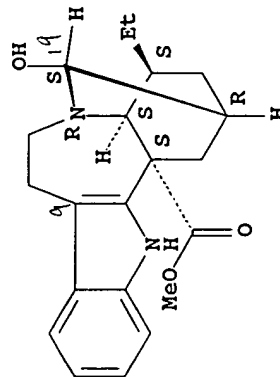
FS STEREOSEARCH

MF C21 H26 N2 O3

LC STN Files: BEILSTEIN*, CA

DES 4:19S.IBOGAMINE
 (*File contains numerically searchable property data)

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 103:160748

REFERENCE 2: 94:157129

L3 ANSWER 4 OF 8 REGISTRY COPYRIGHT 1994 ACS

RN 57511-56-5 REGISTRY

CN ibogamine-18-carboxylic acid, 20-hydroxy-, methyl ester, (4.alpha.,20R)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine-18-carboxylic acid deriv. (9CI)

OTHER NAMES:

CN (-)-19-Epiheyneanine

CN 19-Epiheyneanine

CN 19R-Heyneanine

CN 20-Epiheyneanine

CN Epiheyneanin

CN Epiheyneanine

FS STEREOSEARCH

MF C21 H26 N2 O3

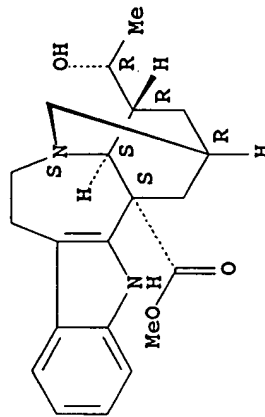
CI COM

LC STN Files:

BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, NAPRALERT, TOXLIT (*File contains numerically searchable property data)

DES 4:4A,20R.IBOGAMINE

Absolute stereochemistry.



22 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 118:124850

REFERENCE 2: 114:58868

REFERENCE 3: 111:17218

REFERENCE 4: 108:167739

REFERENCE 5: 107:95165

REFERENCE 6: 107:93506

REFERENCE 7: 107:46385

REFERENCE 8: 104:213084

REFERENCE 9: 103:211119

REFERENCE 10: 102:201148

L3 ANSWER 5 OF 8 REGISTRY COPYRIGHT 1994 ACS

RN 53508-36-4 REGISTRY

CN Ibogamine-18-carboxylic acid, 19-hydroxy-, methyl ester, (19R) -

(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 6,9-Methano-5H-pyrindo[1',2':1,2]azepino[4,5-b]indole,

ibogamine-18-carboxylic acid deriv. (9CI)

OTHER NAMES:

CN (-)-Eglandine

CN (19R)-Hydroxycoronaridine

CN (3R)-Hydroxycoronaridine

CN Eglandine

FS STEREOSEARCH

DR 77171-01-8

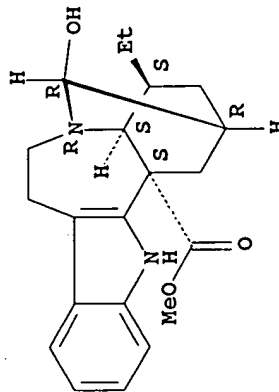
MF C21 H26 N2 O3

LC STN Files: BEILSTEIN*, CA, NAPRALERT

(*File contains numerically searchable property data)

DES 4:19R.IBOGAMINE

Absolute stereochemistry.



7 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 114:58868

REFERENCE 2: 103:160748

REFERENCE 3: 95:147100

REFERENCE 4: 83:1111127
 REFERENCE 5: P 83:97685
 REFERENCE 6: 81:120844
 REFERENCE 7: P 81:91779

13 ANSWER 6 OF 8 REGISTRY COPYRIGHT 1994 ACS
 RN 16671-16-2 REGISTRY

CN Ibogamine-18-carboxylic acid, 16,17-didehydro-9,17-dihydro-9-hydroxy-, methyl ester, (9.alpha.)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 6,9-Methano-8H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine-18-carboxylic acid deriv. (9CI)

CN Coronaridine hydroxyindolenine (8CI)

OTHER NAMES:

CN Hydroxyindolenine-coronaridine

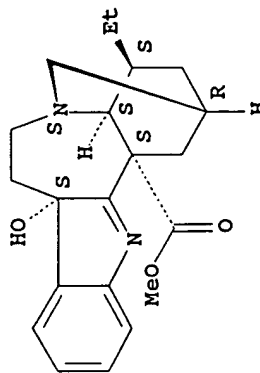
FS STEREOSEARCH

MF C21 H26 N2 O3

LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, NAPRALERT
 (*File contains numerically searchable property data)

DES 4:9A.IBOGAMINE

Absolute stereochemistry.



16 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 120:212597
 REFERENCE 2: 116:55592
 REFERENCE 3: 114:58868
 REFERENCE 4: 109:107714
 REFERENCE 5: 102:163683
 REFERENCE 6: 102:146159

Rs160
 Q4345.43
 Q4415.7.048
 TP248.2.05
 S0451.5.N32

REFERENCE 7: 102:128845

REFERENCE 8: 100:103692

REFERENCE 9: 97:52527

REFERENCE 10: 95:147100

L3 ANSWER 7 OF 8 REGISTRY COPYRIGHT 1994 ACS

RN 4865-78-5 REGISTRY

CN Ibogamine-18-carboxylic acid, 20-hydroxy-, methyl ester, (4.alpha.,20S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine-18-carboxylic acid deriv. (9CI)

CN Heyneanine (7CI)

OTHER NAMES:

CN (-)-Heyneanine

CN Heyneanin

FS STEREOSEARCH

DR 100657-71-4

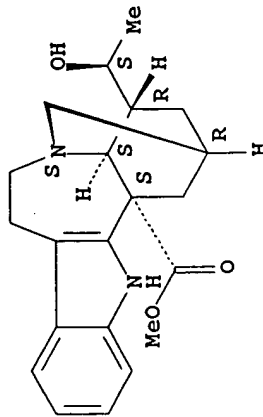
MF C21 H26 N2 O3

LC

STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, NAPRALERT, SPECINFO, TOXLIT

DES 4:4A,20S.IBOGAMINE
(*File contains numerically searchable property data)

Absolute stereochemistry.



30 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 116:55592

REFERENCE 2: 114:58868

REFERENCE 3: 111:17218

REFERENCE 4: 110:189357

REFERENCE 5: 110:111819
 REFERENCE 6: 109:107714
 REFERENCE 7: 107:83746
 REFERENCE 8: 106:116489
 REFERENCE 9: 104:65956
 REFERENCE 10: 102:163683

✓L3 ANSWER 8 OF 8 REGISTRY COPYRIGHT 1994 ACS
 RN 3464-63-9 REGISTRY

CN Ibogamine-18-carboxylic acid, 16,17-didehydro-9,17-dihydr -9-
 hydroxy-12-methoxy-, methyl ester, (9.alpha.)- (9CI) (CA
 INDEX

NAME)

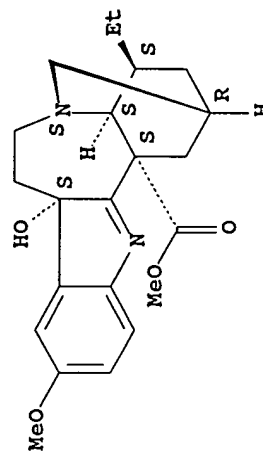
OTHER CA INDEX NAMES:

CN 6,9-Methano-8H-pyrido[1',2':1,2]azepino[4,5-b]indole-6(6aH)-
 carboxylic acid, 7-ethyl-7,9,10,12,13,13a-hexahydro-13a-hydroxy-2-
 methoxy-, methyl ester (7CI)
 CN 6,9-Methano-8H-pyrido[1',2':1,2]azepino[4,5-b]indole,
 ibogamine-18-carboxylic acid deriv. (9CI)
 CN 9H-Voacangine, 9-hydroxy- (8CI)

OTHER NAMES:

CN 7-Hydroxy-1-dehydrovoacangine
 CN Voacangine 7-hydroxyindolenine
 CN Voacangine hydroxyindolenine
 FS STEREOSEARCH
 DR 19779-79-4
 MF C22 H28 N2 O4
 LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, NAPRALERT
 (*File contains numerically searchable property data)
 DES 4:9A.IBOGAMINE

Absolute stereochemistry.



L49 18 S IBOGAMIN# OR HYDROXYIBOGAMIN#
 L50 18 S L48 OR L49
 L51 1 S D15.160./CT AND L50
 L52 0 S L50 AND ADDITION+NT/CT
 L53 2 S L50 AND INTOXICATION+NT/CT
 L54 1 S ALLOIBOGAMINE OR 9 HYDROXY 9 H IBOGAMINE
 L55 3 S L51 OR L53 OR L54
 L56 0 S L50 AND (ALCOHOL ABUSE+NT/CT OR DRUG ABUSE+NT/CT)

FILE 'WPIDS' ENTERED AT 12:33:37 ON 14 OCT 94

L57 7 S 7IBOGAMIN?
 L58 4 S L57 NOT L25

=> fil hca

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FILE COVERS 1967 - 1 Oct 1994 (941001/ED) VOL 121 ISS 14

THE BASIC INDEX NOW INCLUDES ABSTRACT TEXT. SEE NEWS FOR DETAILS.
 'OBI' IS DEFAULT SEARCH FIELD FOR 'HCA' FILE

=> d l38 1-6 bib ab hitrn

⁹L38 ANSWER 1 OF 6 CA COPYRIGHT 1994 ACS
 AN 116:143736 CA
 TI Mechanisms of action of ibogaine and harmaline congeners based on
 radioligand binding studies
 AU Deecher, Darlene C.; Teitler, Milton; Soderlund, David M.; Bornmann,
 William G.; Kuehne, Martin; Glick, Stanley D.
 CS Dep. Pharmacol. Toxicol., Albany Med. Coll., Albany, NY, 12208, USA
 SO Brain Res. (1992), 571(2), 242-7
 DT CODEN: BRREAP; ISSN: 0006-8993
 LA Journal
 AB English

Assays using radioligands were used to assess the actions of
 ibogaine and harmaline on various receptor types. Ibogaine
 congeners showed affinity for opiate receptors whereas harmaline and
 harmine did not. The K_i for coronaridine was 2.0 μ M at
 μ -opiate receptors. The K_i for coronaridine and tabernanthine
 at the δ -opiate receptors were 8.1 and 3.1 μ M, resp.
 Ibogaine, ibogamine, coronaridine, and tabernanthine had
 K_i values of 2.08, 2.6, 4.3 and 0.15 μ M, resp., for
 κ -opiate receptors. Long-lasting, dose-dependent behavioral
 effects of ibogaine have been reported. The possibility that these
 effects were due to irreversible binding properties of ibogaine at
 κ -receptors was considered; however, radioligand wash expts.
 showed a rapid recovery of radioligand binding after one wash. A
 voltage-dependent sodium channel radioligand demonstrated K_i values
 in the μ M range for all drugs tested. Using radioligand binding
 assays and/or $^{36}\text{Cl}^-$ uptake studies, no interaction of ibogaine or
 harmaline with the GABA receptor-ionophore was found. The
 κ -activity of ibogaine (or an active metabolite) may be

responsible for its putative anti-addictive properties whereas the tremorigenic properties of ibogaine and harmaline may be due to their effects on sodium channels.

IT 481-87-8, Ibogamine

(receptor affinity for, mechanism of action in relation to)

138

AN 116:100980 CA

TI A rapid method for interrupting or attenuating poly-drug dependency

IN Lotsof, Howard S.
PA NDA International, Inc., USA
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2

PI WO 9118609 A1 911212

DS W: CA, JP

AI WO 91-US3781 910530

PRAI US 90-531100 900531

DT Patent

LA English

AB The administration of ibogaine, ibogamine, tabernantheine, or their nontoxic salts interrupts the physiol. and psychol. aspects of poly-drug dependency to heroin, cocaine, alc., nicotine, caffeine, amphetamine, desoxyephedrine, or methadone in combinations thereof. A single treatment or series of treatments may be effective for 1-18 mo or longer. A patient addicted to alc., cocaine, and heroin was treated with ibogaine; a single dose of ibogaine at 15 mg/kg body wt. completely interrupted heroin and cocaine use and diminished alc. use by 50-80 % on a daily basis.

IT

481-87-8, Ibogamine 481-87-8D,

Ibogamine, salts with tannic acid

(drug dependence treatment with)

138

AN 116:17031 CA

TI Rapid method for interrupting or attenuating the nicotine/tobacco

IN Lotsof, Howard S.
PA NDA International, Inc., USA
SO U.S., 4 pp.
CODEN: USXXAM

PI US 5026697 A 910625

AI US 90-530263 900530

DT Patent

LA English

AB The administration to a nicotine or tobacco addict of ibogaine, ibogamine, or tabernantheine or nontoxic salts of these alkaloids of the family Apocyanaceae interrupts the physiol. and psychol. aspects of nicotine or tobacco dependency. A single treatment or series of treatments may be effective for .gtoreq.1-18 mo. Dose ranges are 1-60 mg/kg for oral, rectal infusion, or suppository administration of the above alkaloids. Thus, a subject who was smoking .gtoreq.2 packs of filter cigarettes per day was

administered a single dose of 15 mg ibogaine/kg. The subject suffered no nicotine withdrawal and has not smoked cigarettes for >24 mo., at which time tracking ceased.

IT 481-87-8, Ibogamine 481-87-8D,
Ibogamine, tannic acid salts
(for tobacco/nicotine dependency treatment)

/L38 ANSWER 4 OF 6 CA COPYRIGHT 1994 ACS

AN 109:122005 CA

TI Non-amphetaminic central stimulation by alkaloids from the ibogane and vobasine series

AU Bert, Maryse; Marcy, Rene; Quermonne, Marie Anne; Cotellet, Michel; Koch, Michel

CS Dep. Pharmacogn., UER Sci. Pharm., Caen, F-14000, Fr.

SO Planta Med. (1988), 54(3), 191-2

DT CODEN: PLMEAA; ISSN: 0032-0943

LA Journal

AB English

Ibogane alkaloids I (R1 and R2 = H, OMe; R3 = H, CH2OH, CO2Me, CH2OAc, or vobasiny) had a very high arousal activity in mice. Similarly, a CNS-stimulating activity was demonstrated for vobasine alkaloids II (R = H; R1 = OH, S(CH2)2NH2; RR1 = O; R2 = H, Me). The influence of certain substituents was shown; methoxy substitution increased the activity, while it was lowered by methoxycarbonyl substitution.

IT 481-87-8D, Ibogamine, derivs.

(central nervous system-stimulant activity
of, structure in relation to)

/L38 ANSWER 5 OF 6 CA COPYRIGHT 1994 ACS

AN 75:6166 CA

TI Iboga alkaloid derivatives as central nervous system stimulants

IN Sallay, Stephen I.

PA am homme

SO U.S., 7 pp.

PI CODEN: USXXAM

AI US 3557126 710119

DT US 690814

LA Patent

AB English

A synthesis of ibogamine (I) is described via II-XV in which the indole ring closure of cis-9-ethyl-octahydro-1,7-methano-1H-benzazepin-5(4H)-one as the last step provides versatility in the prepn. of Iboga alkaloids.

0/L38 ANSWER 6 OF 6 CA COPYRIGHT 1994 ACS

AN 73:131198 CA

TI Central-nervous-system stimulant derivatives of

IN Iboga alkaloids and Iboga intermediates

PA Sallay, Stephen I.

SO American Home Products Corp.

DT U.S., 8 pp.

PI CODEN: USXXAM

US 3516989 700623

US 671002

Patent

English

PI

AI

DT

LA

AB

trans-1,3-Hexadiene (194 g) in 2500 ml benzene was refluxed for 2 hr with 286 g p-quinone to give d,l-cis-5-beta-ethyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (I), m. 46-8.degree.. I was reduced with HOAc and Zn dust to give d,l-cis-5-beta-ethyl-2,3,4a,5,8,8a-hexahydro-1,4-naphthoquinone (II), m. 71-3.degree.. II (247 g) in 500 ml CH₂Cl₂ and 600 ml HOAc was treated with 88 g HOCH₂CH₂OH in 360 ml HOAc and 186 g BF₃.Et₂O in 250 ml HOAc to give d,l-cis-5'-beta-ethyl-2',3',4'a,5',8',8'a-hexahydrospiro[1,3-dioxolane-2,1'(4'H)-naphthalen]-4'-one (III), b0.01 104.degree.. III was heated to 60.degree. with 1 mole equiv. of hydroxylamine acetate in MeOH (from 102 g NH₂OH.HCl and 118 g NaOAc) to give 260 g III oxime (IV), m. 125-6.degree.. IV (100 g) in pyridine was treated at 75.degree. with 76 g p-Mec6H₄SO₂Cl to give 83.8 g d,l-cis-9-beta-ethyl-3,4,5a,6,7,8,9a-hexahydrospiro[5H-1-benzazepino-5,2'-(1,3)-dioxolane]-2(1H)-one (V), m. 144-5.degree.. V (50 g) was oxidized with 0.2 mole m-ClC₆H₄CO₂OH to give d,l-cis-7.alpha.,8.alpha.-epoxy-9-beta-ethyl-3,4,5a,6,7,8,9,9a-octahydrospiro[5H-1-benzazepino-5,2'-(1,3)-dioxolane]-2(1H)-one (VI), m. 170-1.degree.. Redn. with LiAlH₄ converted VI to d,l-cis-9-beta-ethyl-3,4,5a,6,7,8,9a-octahydro-7a-hydroxyspiro[5H-1-benzazepino-5,2'-(1,3)-dioxolane]-2(1H)-one (VII), m. 180-1.5.degree.. VII (9 g) in pyridine was oxidized with a CrO₃-pyridine complex (from 8.0 g CrO₃ and 120 ml pyridine, below 25.degree.) to give 7.6 g d,l-cis-9-beta-ethyl-3,4,5a,6,7,8,9a-hexahydrospiro[5H-1-benzazepino-5,2'-(1,3)-dioxolane]-2,7(1H)-dione (VIII), m. 220.degree.. VIII (2.6 g) in 100 ml Me₂SO was treated with triphenylphosphonium methyliide (prepd. dimethylsodium from Me₂SO and PPh₃MeBr) and the mixt. heated to 30-40.degree. for a few hr to give 2.14 g d,l-cis-9-ethyl-3,4,5a,6,7,8,9a-octahydro-7-methylenespiro[5H-1-benzazepine-5,2'-(1,3)-dioxolane]-2(1H)-one (IX), m. 196-7.degree.. the mixt. kept overnight. The mixt. was then treated with 4 ml 10% NaOH and 2 ml 50% H₂O₂ and excess H₂O₂ decompd. with Pd-C to give d,l-cis-9-ethyl-3,4,5a,6,7,8,9a-octahydro-7-hydroxymethylspiro[5H-1-benzazepine-5,2'-(1,3)-dioxolane]-2(1H)-one (X). This lactam in THF was reduced with LiAlH₄ to give d,l-cis-9-ethyl-3,4,5a,6,7,8,9a-octahydro-7-hydroxymethylspiro[5H-1-benzazepine-5,2'-(1,3)-dioxolane]-2(1H)-one (XI) as a gum. XI (11.6 g) was treated with N LiOH and 12 g carbobenzoxy chloride at 10.degree. to form d,l-cis-9-ethyl-3,4,5a,6,7,8,9a-octahydro-7-hydroxymethylspiro[5H-1-benzazepine-5,2'-(1,3)-dioxolane]-1(2H)-carboxylic acid benzyl ester (XII). XII was treated with p-Mec6H₄SO₂Cl to form the tosyl ester of XII, which was treated with HOAc and HBr to give the hydrobromide of XII. This compd. (1 g) in NaOH was extd. with CH₂Cl₂, the base refluxed for 10 hr in isoamyl alc., and the resulting compd. treated with HBr gas to give d,l-cis-9-ethyl-3,4,5a,6,7,8,9a-octahydro-7-hydroxymethylspiro[5H-1-benzazepine-5,2'-(1,3)-dioxolane]-2(1H)-one (XIII). Treatment of this salt with H₂SO₄ followed by 0.3 ml PhNH₂ gave ibogamine.

=>

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FILE COVERS 1974 TO 6 Oct 1994 (941006/ED)

=> d 155 1-3 bib ab

- 0 L55 ANSWER 1 OF 3 EMBASE COPYRIGHT 1994 ELSEVIER SCI. B.V.
AN 94278996 EMBASE
TI Effects of iboga alkaloids on morphine and cocaine
self-administration in rats: Relationship to tremorigenic effects
and to effects on dopamine release in nucleus accumbens and
striatum.
AU Glick S.D.; Kuehne M.E.; Raucci J.; Wilson T.E.; Larson D.; Keller
R.W. Jr.; Carlson J.N.
CS Dept. Pharmacology Toxicol. (A-136), Albany Med. Coll. Capital
Districts, Ctr. Drug Abuse Res. and Treatment, Albany, NY 12208,
United States
SO BRAIN RES., (1994) 657/1-2 (14-22).
ISSN: 0006-8993 CODEN: BRREAP
CY Netherlands
DT Journal
FS 030 Pharmacology
040 Drug Dependence, Alcohol Abuse and Alcoholism
037 Drug Literature Index
LA English
SL English
AB Ibogaine, a naturally occurring alkaloid, has been claimed to be
effective in treating addiction to opioid and stimulant drugs and
has been reported to decrease morphine and cocaine
self-administration in rats. The present study sought to determine if
other iboga alkaloids, as well as the chemically related harmala
alkaloid harmaline, would also reduce the intravenous
self-administration of morphine and cocaine in rats. Because both
ibogaine and harmaline induce tremors, an effect that may be
causally related to neurotoxicity in the cerebellar vermis, the
temorigenic activities of the other iboga alkaloids were assessed.
Lastly, in view of the involvement of the dopaminergic mesolimbic
system in the actions of drugs of abuse, the effects of some of the
iboga alkaloids on extracellular levels of dopamine and its
metabolites in the nucleus accumbens and striatum were determined.
All of the tested alkaloids (i.e., ibogaine, desethylcoronaridine,
S-coronaridine, R- and S-ibogamine, desethylcoronaridine,
and harmaline) dose-dependently (2.5-80 mg/kg) decreased morphine
and cocaine intake in the hour after treatment; decreases in
morphine and cocaine intake were also apparent the day after
administration of some but not all of these alkaloids (i.e.,
ibogaine, tabernanthine, desethylcoronaridine, and the R-isomers of
coronaridine and ibogamine). In some rats, there were
persistent decreases in morphine or cocaine intake for several days
after a single injection or after two or three weekly injections of
one or another of these alkaloids; R-ibogamine produced
such effects more consistently than any of the other alkaloids. At

the doses used to assess effects on drug self-administration, ibogaine, tabernanthine, desethylcoronaridine and harmalin all induced tremors for at least 2-3 h; both enantiomers of both coronaridine and ibogamine induced very weak or no tremors. Using in vivo microdialysis, the effects of the R- and S-enantiomers of coronaridine and ibogamine on extracellular dopamine levels in the nucleus accumbens and striatum were compared. The R-enantiomers decreased dopamine levels in both brain regions whereas the S-enantiomers produced no significant changes in dopamine levels in either region. The results of this study indicate that the 'anti-addictive' and tremorigenic effects of the iboga alkaloids can be dissociated and that long-term effects of these alkaloids on drug self-administration appear to be related to initial decreases in dopaminergic activity in specific brain areas.

✓L55 ANSWER 2 OF 3 EMBASE COPYRIGHT 1994 ELSEVIER SCI. B.V.

AN 84016445 EMBASE
TI Tertiary indole alkaloids of Tabernaemontana dichotoma seeds.
AU Perera P.; Sandberg F.; Van Beek T.A.; Verpoorte R.
CS Dep. Pharmacogn., Biomed. Cent., Univ. Uppsala, S-75123 Uppsala, Sweden
SO PLANTA MED., (1983) 49/1 (28-31).
CODEN: PLMEAA
CY Germany, Federal Republic of
LA English

L55 ANSWER 3 OF 3 EMBASE COPYRIGHT 1994 ELSEVIER SCI. B.V.

AN 78308335 EMBASE
TI [Alkaloids of Tabernanthe iboga].
AU LES ALCALOÏDES DE L'IBOGA (TABERNANTHE IBOGA H.Bn.).
AU Gagnault J.C.; Delourme-Houde J.
CS Cent. Rech. Roussel Uclaf Romainville, Paris, France
SO FITOTERAPIA, (1977) 48/6 (243-265).
CODEN: FTRPAE
CY Italy
LA French

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L58 ANSWER 1 OF 4 COPYRIGHT 1994 DERWENT INFORMATION LTD
 AN 71-26418S [15] WPIDS
 TI Cis-9-alkyloctahydro-1,7-methano-1h-1-benz- - azepin-5-(4h)-ones,
 intermediates for iboga.
 DC B02
 PA (AMHP) AMERICAN HOME PROD CORP
 CYC 1
 PI US 3574220 A (7115)*
 PRAI US 67-671966 671002; US 69-870997 690814
 IC C07D039-00
 AN 71-26418S [15] WPIDS
 AB US 3574220 A UPAB: 930831
 Cis-9-alkyloctahydro-1,7-methano-1h-1-benzazepin-5-(4H)-ones,
 intermediates for iboga alkaloids. Cpds. of formula: - (where R1 is
 1-6C alkyl), are converted to iboga alkaloids, which are CNS
 stimulants, by condensation with phenylhydrazine or ring-substituted
 derivs. thereof. The cpds. are prepd. by cyclization of
 cis-9-alkyl-decahydro-7-tosyloxymethyl-5H-benzazepin-5-ones. Thus
 dl-cis-9-ethyldecahydro-7-tosyloxymethyl-5H-benzazepin-5-on is
 refluxed in iso-amyl alcohol to give, after gasification,
 dl-cis-9-ethyloctahydro-1,7-methano-1h-1-benzazepin-5(4H)-one,
 which, on condensation with phenylhydrazine, gives ibogamine

L58 ANSWER 2 OF 4 COPYRIGHT 1994 DERWENT INFORMATION LTD
 AN 66-35100F [00] WPIDS
 TI (A) Cpds. (I) R - H or lower alkyl (B) Method for
 isoquinuclidine alkaloids (X). Anti-tumour, anti-protozoals,
 analeptics, analgesics, and ant.

DC B02
 PA (SHIO) SHIONOGI & CO LTD
 CYC 8

PI NL 6807826 A 681203 (6800)*
 FR 1572766 A (6801)
 JP 45039270 B (7049)
 JP 46004180 B (7105)
 GB 1236488 A (7124)
 CH 510669 A (7141)
 CH 511233 A (7141)
 US 3639408 A (7210)
 CH 518940 A (7220)
 CA 913103 A (7245)
 CA 913104 A (7245)
 US 3716528 A (7309)
 DE 1770561 A 711104 (8523)

PRAI JP 67-35647 670603; JP 68-7620 680207
 IC C07D039-06
 AN 66-35100F [00] WPIDS
 AB NL 6807826 A UPAB: 930831

(A) Cpds.
 (I) R = H or lower alkyl
 (B) Method for isoquinuclidine alkaloids (X).
 Anti-tumour, anti-protozoals, analeptics, analgesics, and

antivirals.

- (a)
 (b) R' and R2 = H or lower alkyl
 X = an organic acid residue, e.g. p-Me.C6H4SO2
 Y = lower alkyl
 Z and Z' = H, lower alkyl, lower alkyl or halogen.
 desethylibogamine, m.p.184-6.

✓L58
 AN
 TI
 DC
 PA
 CYC
 PI

ANSWER 3 OF 4 COPYRIGHT 1994 DERWENT INFORMATION LTD

66-02183F [00] WPIDS
 Ester alkaloids of indole series.

B00

3 (GEIG) GEIGY AG

DE 1132561 A (6800)*
 JP 38006478 B (6801)
 NL 249100 B (6801)

AN 66-02183F [00] WPIDS

AB DE 1132561 A UPAB: 930831

Ester alkaloids of indole series wherein the benzene ring may be substd. by methoxy and R is lower alkyl) or the indolenine are decarboxylated by heating with a base R1 - NH2 (where R1 is amino alkylamino, aralkylamino, cycloalkylamino, alkyl, in the presence of a solvent and opt. in N2 atmosphere. Suitable starting materials are voacangin, isovoacangin, voacristin, and 12:13-dimethoxy-coronaridin, and the base may be hydrazine or hydrazine hydrate. The 12:13-dimethoxy-ibogamin. obtd. from

12:13-dimethoxy-coronaridin is new cpd. which potentiates analgetics, such as morphine and aminopyrin and it also shows analgetic activity.

✓L58
 AN
 TI
 DC
 PA
 CYC

ANSWER 4 OF 4 COPYRIGHT 1994 DERWENT INFORMATION LTD

66-02181F [00] WPIDS
 12 13-dimethoxyibogamine.

B00

4 (GEIG) GEIGY A-G JR

DE 1134082 A (6800)*
 CH 372291 A (6801)
 GB 924042 A (6801)
 NL 249096 B (6801)

AN 66-02181F [00] WPIDS

AB DE 1134082 A UPAB: 930831

New 12:13-dimethoxy-ibogamine is an isoquinuclidine alkaloid

effective against the effect of reserpine in mice. It is prepared by treating 12:13-dimethoxycoronaridine (extracted from the stem bark of Conopharyngia durissima Staff) with a soln. of an alkali hydroxide in an alcohol and decarboxylating the intermediate product obtained by heating in an acid medium. In an Example, 2 pt. 12:13-dimethoxycoronaridine and 50 pt. 20% methanolic KOH are heated under reflux for 6 hrs., pref. under N2. The soln. is then cooled, methanol removed under vacuum, the

residue dissolved in water, acidified with HCl (pH < 2), heated for 2 hrs. at 80-90 deg.C, cooled, made alkaline with NH₃, the pptd. base filtered, and recrystallised from methanol to give 0.85 pt. of product, m.pt. 136 deg.C. On recrystallisation from ether-petroleum ether a crystalline 12:13-dimethoxy-ibogamine of m.pt. 146 deg.C is obtained.